

Application No.: 09/928,048

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**REMARKS**

Claims 1-9 and 12-25 are pending. Claims 1-6 and 12-16 are withdrawn from consideration, and claims 7-9 and 17-25 are rejected. Claims 12-16 are cancelled, and claims 1, 7 and 17 are amended herein. Support for the present claim amendments can be found throughout the specification and claims as originally filed, for example, at page 2, first (non-full) paragraph; and page 4, last paragraph.

The amendments are made solely to promote prosecution without prejudice or disclaimer of any previously claimed subject matter. With respect to all amendments, the Applicant has not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. The Applicant expressly reserves the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

The Applicant has carefully considered the points raised in the Office Action and believe that the Office's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

**Rejections under 35 U.S.C. § 112, first paragraph****Written Description**

Claims 7-9 and 17-25 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Applicant respectfully traverses this ground for rejection.

The Office asserts that the Applicant "does not disclose what this CIP fragment is." In response, the Applicant asserts that the intended meaning of the terms "CIP" or "CIP fragment" are set forth in the specification at page 4, third paragraph. Although in abbreviated format, the

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specification indicates that the terms "CIP" or "CIP fragment" refer to a contiguous portion of human PTH having an amino acid sequence set forth in SEQ ID NO:3 (PTH<sub>1-84</sub>), wherein the CIP has the following characteristics: a) the N-terminal amino acid residue of the CIP starts at any position spanning from position 2 through position 34 of the PTH<sub>1-84</sub>; and b) the C-terminal amino acid residue of the CIP ends at position 84 of the PTH<sub>1-84</sub>. This description includes and refers to a set of peptides as representative of a CIP fragment, such as PTH<sub>2-84</sub>, PTH<sub>3-84</sub>, PTH<sub>4-84</sub>, PTH<sub>5-84</sub>, PTH<sub>6-84</sub>, PTH<sub>7-84</sub>, PTH<sub>8-84</sub>, PTH<sub>9-84</sub>, PTH<sub>10-84</sub> . . . PTH<sub>28-84</sub>, PTH<sub>29-84</sub>, PTH<sub>30-84</sub>, PTH<sub>31-84</sub>, PTH<sub>32-84</sub>, PTH<sub>33-84</sub>, up to and including PTH<sub>34-84</sub>. In essence, the term "CIP" or "CIP fragment," as used in the present application means the same thing as if the Applicant had listed out each individual CIP peptide between the listed boundaries. This set of polypeptides is small, clear and has definite boundaries.

Nevertheless, the present claims have been limited to the measurement of a specific polypeptide comprising PTH<sub>7-84</sub>. This polypeptide comprises a PTH antagonist and falls within the small and defined set of CIP/CIP fragments described above. Moreover, further support for this specific polypeptide can be found in the reference to LePage, R., et al. (*Clin. Chem.* (1998) 44:805-10) in the specification at page 2. This publication was incorporated by reference in the present application and discusses the interference of synthetic PTH<sub>7-84</sub> in assays for whole PTH and hypothesizes about its physiological activity. It was later verified that PTH<sub>7-84</sub>, as a PTH antagonist, effects internalization, and ultimately leads to a down regulation, of the 1-84 PTH/PTHrp receptor, without concomitant activation. See Sneddon et al., *J. Biol. Chem.* (2003) 278(44):43787-96 (attached hereto at **Exhibit A**). In addition, PTH<sub>7-84</sub> generally binds and activates a C-terminal receptor that is *independent* of the 1-84 PTH/PTHrp receptor. See P. Divieti, et al., *Endocrinology* (2002) 143(1):171-6 (attached hereto at **Exhibit B**).

Accordingly, the Applicant respectfully submits that the written description requirement has been met, especially in view of the present claim amendments. A specific CIP/CIP fragment that is supported in the application, as filed, is identified in the present methods. Withdrawal of this rejection is respectfully requested.

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### Enablement

Claims 7-9 and 17-25 were rejected under 35 U.S.C. § 112, first paragraph, for allegedly not enabling any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims. The Applicant respectfully traverses this rejection.

In this rejection the Office is again concerned that "[t]he disclosure fails to teach what the cyclase inhibiting parathyroid hormone fragment is." Office Action, page 4, first full paragraph. However, the Office further explains that "[b]ecause the disclosure fails to teach what the fragment is, one of ordinary skill in the art would not be able to generate an antibody for the fragment without undue experimentation and thus one would have a low level of predictability in the art." *Id.* (in the second full paragraph). The Office is additionally concerned that the description supposedly provides no working examples. *Id.* Finally, the Office indicates that since one of skill in the art purportedly does not know what the CIP fragment is, then one could not generate an antibody for the peptide sequence in CIP without undue experimentation. *Id.*

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. Time and difficulty are not determinative of undue experimentation if the experimentation is routine. See *PPG Indus., Inc. v. Guardian Indus. Corp.*, 75 F.3d 1558, 1564, 37 USPQ2d 1618, 1623 (Fed. Cir. 1996); *In re Wands*, 858 F.2d 731, 736-37, 8 USPQ2d 1400, 1403-07 (Fed. Cir. 1988) (applying this principle in the context of monoclonal antibody production); and MPEP §§ 2164.01, 2164.06. As for the concern regarding working examples, it is accepted that an application need not describe what is already known in the art. See, e.g., *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 221 USPQ 481 (Fed. Cir. 1984).

Methods for generating antibodies to a specifically provided polypeptide sequence, and in accordance with the present claims, are well known in the art.

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Accordingly, the Applicant submits that the pending claims fall within the subject matter that is enabled and described by the specification. In particular, a specific CIP/CIP fragment comprising a PTH antagonist is identified. Accordingly, the Applicant respectfully requests reconsideration and withdrawal of this rejection.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 7-9 and 19-25 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

The claims are amended herein to identify a specific CIP/CIP fragment and to remove the language objected to by the Office. Accordingly, the Applicant respectfully requests reconsideration and withdrawal of the present rejection.

Restriction Status

As requested by the Office, the Applicant indicates that, as used in the present application, and specifically limited thereto, the terms "CIP" and "CIP fragment" are the same and are not patentably distinct.

CONCLUSION

The Applicant believes that all issues raised in the Office Action have been properly addressed in this response. Accordingly, reconsideration and allowance of the pending claims is respectfully requested. If the Examiner feels that a telephone interview would serve to facilitate resolution of any outstanding issues, the Examiner is encouraged to contact Applicant's representative at the telephone number below.

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In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 532212001500.

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Respectfully submitted,

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